Remarks

Claims 1-7, 20, 21, 46-83 are pending. Claims 8-19 have been canceled. Claims 22-45 were not entered. Claims 1 and 46 have been amended. Claims 70-83 are newly added. Claim 1 has been amended to replace "coding region" with "sequence" and to recite "the riboswitch regulates expression of the sequence." Support for this amendment can be found throughout the specification and in particular in original claim 1 and on page 4, lines 8-14. Claim 46 was amended to recite "wherein the riboswitch comprises an aptamer domain and an expression platform domain." Support for this amendment can be found throughout the application and in particular in original claim 2.

Support for new claim 70 can be found at least in original claims 1 and 2, on page 4, lines 8-14, and on page 42, lines 1-4. Support for new claims 71 and 75 can be found at least in original claim 1. Support for new claim 72 can be found at least in original claim 1 and in the sentence bridging pages 35 and 36. Support for new claim 73 can be found at least in original claim 1, on page 4, lines 8-14, on page 30, lines 6-14, from page 31, line 31, to page 33, line 31, from page 106, line 13, to page 107, line 9, and from page 110, line 27, to page 111, line 3. Support for new claim 74 can be found at least in original claims 1 and 2, in the sentence bridging pages 35 and 36, and on page 42, lines 1-4. Support for new claim 76 can be found at least in original claim 1, in the sentence bridging pages 35 and 36, on page 4, lines 3-4, and on page 29, lines 16-19. Support for new claim 77 can be found at least in original claim 1, on page 4, lines 3-4, and on page 29, lines 16-19. Support for new claim 78 can be found at least in original claims 1 and 2, on page 4, lines 8-14, and in the sentence bridging pages 3 and 4. Support for new claim 79 can be found at least in original claims 1 and 6, on page 4, lines 8-14, and on page 37, lines 6-7. Support for new claim 80 can be found at least in original claim 1. Support for new claim 81 can be found at least in the sentence bridging pages 35 and 36. Support for new claim 82 can be found at least on page 74, lines 26-29. Support for new claim 83 can be found at least on page 4, lines 8-14.

Applicants note with appreciation the withdrawal of the prior rejection under 35 U.S.C. § 112, first paragraph.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-7, 20, 21 and 46-69 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

1. The rejection states that the mentioned claims are indefinite allegedly because the metes and bounds of "a coding region" cannot be determined. Applicants disagree.

35 U.S.C. § 112, second paragraph, requires that the claims particularly point out and distinctly claim what applicant considers to be his invention. This standard is applied through the eyes of those of skill in the art. If the claim language would be sufficiently clear and precise to those of skill in the art, then the claim meets the requirements of 35 U.S.C. § 112, second paragraph. Regarding clarity and precision of the claims, it is only required that the claims define the patentable subject matter with reasonable clarity. Absolute precision is not required.

The present rejection alleges that the meets and bounds of the term "coding region" is not clear. As an example, the rejection posits that a "coding region" could encompass RNA encoding a single amino acid. Applicants first note that this example does not fit within a reasonable interpretation of the term "coding region." A coding region is a stretch of nucleotides that encodes a protein or peptide. That is, a nucleic acid sequence that happens to have nucleotides that match the sequence of codons in the genetic code is not a "coding region" unless it is capable of being translated into a protein or peptide. This is illustrated by the fact that those of skill in the art have a completely separate term, "open reading frame," to define a stretch of nucleotides that match the sequence of codons in the genetic code but is not necessarily capable of being translated into a protein or peptide (because it lacks a start codon or is not downstream from a promoter, for example). When this definition of coding region is applied to the interpretation alleged in the rejection it becomes clear that no coding region could be a nucleotide sequence matching the sequence of a codon for a single amino acid at least because it does not code for any protein or peptide that could be synthesized. For example, no peptide bond could be formed between a growing amino acid chain and an amino acid where only one amino acid was specified by such an alleged "coding region." For at least this reason, the basis

of the indefiniteness of the term alleged in the rejection is inconsistent with the definition of coding region. Accordingly, the rejection fails to establish that the claims do not comply with the requirements of 35 U.S.C. § 112, second paragraph.

Applicants next note that those of skill in the art are familiar with the well known term "coding region." The term coding region is extensively used in the fields of genetics and molecular biology and appears in, for example, general textbooks on these subjects. As an example, Applicants note that the textbook "Essential Cell Biology – An Introduction to the Molecular Biology of the Cell" (Alberts, B.; Bray, D.; Johnson, A.; Lewis, J.; raff, M.; Roberts, K.; Walter, P., Garland Pub, Inc, New York & London, 1998) uses the term "coding region" and clearly indicates what the term means. In Chapter 7, Alberts et al. discuss the process of DNA→protein wherein coding region and coding sequence are clearly defined. On pages 220, figure 7-13 (a copy of which is submitted with this Response), Alberts et al. defines coding region as "[a] single stretch of uninterrupted nucleotide sequence that encodes the amino acid of a protein" (for a bacterial gene) and notes that "the coding sequence of most eucaryotic genes (*exons*) are interrupted by noncoding sequences (*introns*)." The case of exons and introns in eucaryotic genes is particularly telling. Only the exon sequences are capable of being translated into a protein. Even if the introns contain sequences of codons or open reading frames (and many introns do contain open reading frames), such sequences of codons or open reading frames are not considered coding regions. Thus, the clear definition and understanding by those of skill in the art of the term "coding region" excludes sequences of single codons and open reading frames that are not capable of being translated into a protein. For at least this additional reason the claims meet the requirements of 35 U.S.C. § 112, second paragraph.

Applicants also note that those of skill in the art would not find the term "coding region" to be indefinite in its meaning. As noted above, it is a well known term in genetics and molecular biology that appears in general textbooks on this subject. Given this, it cannot be said that those of skill in the art would not understand what the term means or what are its metes and bounds. This is all that 35 U.S.C. § 112, second paragraph, requires. For at least this additional reason the claims do not violate the requirements of 35 U.S.C. § 112, second paragraph. For all

of the above reasons, Applicants submit that the claims are clear and definite and respectfully request withdrawal of the rejection.

Notwithstanding the above, Applicants have amended claim 1 to eliminate recitation of "coding region." Thus, for at least this reason, the present rejection is moot.

2. The rejection also states that it is unclear "whether the riboswitch in claim 1 regulates expression of the RNA encoding the entire regulatable gene expression construct (i.e. the riboswitch and the coding region), or only regulates the expression of the operably linked coding region." Applicants first note that it is clear from the specification and the claims themselves that the coding region is what is regulated by the riboswitch. First, the application is replete with discussion and description of riboswitches regulating, for example, gene expression, RNA expression, and expression of proteins encoded by RNA-containing riboswitches. Further, claim 1 stated that "the riboswitch regulates expression of the RNA." Thus, it is clear that the riboswitch is regulating the coding region that was recited in claim 1 and not the riboswitch itself. It is not seen how those of skill in the art could arrive at a different conclusion and for this reason the interpretation suggested in the rejection is unreasonable. For at least this reason, the example of alleged indefiniteness in the claims is an unreasonable interpretation of the claim language.

An analogy further illustrates why the interpretation in the rejection is unreasonable. It is common to refer to gene expression and expression of genes. Although genes include promoters and although those promoters regulate gene expression, those of skill in the art would not consider that the promoter is regulating "expression" of the promoter itself. Promoters are not "expressed" and those of skill in the art would not consider that the term "expression" would be used in that way. Those of skill in the art understand that a statement such as "the promoter regulates expression of the gene" indicates that the promoter regulates transcription of the gene and other facets of gene expression (translation of the transcript, for example) but not that the promoter is somehow regulating itself even through the promoter is a part of the gene. Analogously, the statement "the riboswitch regulates expression of the RNA" indicates that the riboswitch regulates, for example, transcription and/or translation of the RNA but not that the

riboswitch is somehow regulating itself even through the riboswitch is a part of the RNA. For at least this additional reason, the example of alleged indefiniteness in the claims is an unreasonable interpretation of the claim language.

Applicants also note that the use of the word "expression" in the claim language at issue makes the interpretation of the claim language in the rejection even more unreasonable. The claims did not recite "the riboswitch regulates the RNA." Rather, the claims recited "the riboswitch regulates expression of the RNA" (emphasis added). Thus, it is clear that it is the expression of the RNA that is being regulated. In this case, those of skill in the art would understand that it is not the RNA or the riboswitch that is being regulated but rather the expression of the RNA. For at least this additional reason, it is clear that the claims cannot be interpreted as the riboswitch regulating the riboswitch. For all of the above reasons, Applicants submit that the claims are clear and definite and respectfully request withdrawal of the rejection.

Notwithstanding the above, Applicants have amended the claims to recite that the riboswitch is operably linked to a sequence and that the riboswitch regulates expression of the sequence. Accordingly, for at least this reason the present rejection is moot.

Rejection Under 35 U.S.C. § 102

Claims 1-7, 20, 47, 48, 50, 51, 53, 54, 56, and 57 were rejected under 35 U.S.C. § 102(a) as being anticipated by Breaker (Curr. Opin. Biotech., 13: 31-39, Feb. 1, 2002). Applicants respectfully traverse this rejection to the extent it is applied to the claims as amended.

For a rejection to be properly founded under 35 U.S.C. § 102(a) the prior art, in this case Breaker, has to achieve at least two criteria: (1) "[A] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California* 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (fed. Cir. 1987), and (2) also, the law has long settled that a prior art reference cannot anticipate an invention unless the reference is enabling. As the Supreme Court explained in *Seymour v. Osborne,* 78 U.S. (11 Wall.) 516, 555 (1870):

> Patented inventions cannot be superseded [i.e., anticipated]…unless the description and drawings [of the reference] contain and exhibit a substantial representation of the patented improvement in such full, clear and exact terms as

> to enable any person skilled in the art or science to which it appertains to make, construct and practice the invention to the same practical extent as they would be enabled to so if the information was derived from a prior patent. Mere vague and general representations will not support such a defense.

The rule is not controversial and has been further established in other cases such as: *Paperless Accounting Inc v Bay Area Rapid Transit Sys.*, 231 USPQ 649, 653 (Fed. Cir. 1986), (citations omitted).

Applicants submit that Breaker fails to meet the requirements for a rejection under 35 U.S.C. § 102(a). The present rejection is based on the allegation that the term "coding region" can reasonably be interpreted to encompass "coding regions" that encode one or two amino acids, that the ribozymes of Breaker allegedly contain such short "coding regions," and that therefore the claims allegedly encompass such ribozymes of Breaker. Applicants disagree. Applicants first note that a coding region cannot comprise the sequence of a single codon. As discussed above in relation to the rejection under 35 U.S.C. § 112, second paragraph, a coding region must be capable of being translated into a protein or peptide. The ribozymes of Breaker, however, have none of the features of an RNA that can be translated. Thus, even if a ribozyme of Breaker happened to include a short open reading frame, it would not constitute a coding region because it would not be capable of being translated into a protein or peptide. For at least this reason, Breaker fails to disclose every feature of claims 1-3, 20, 47, 48, 50, 51, 53, 54, 56, and 57. Accordingly, for at least these reasons, Breaker fails to anticipate claims 1-3, 20, 47, 48, 50, 51, 53, 54, 56, and 57.

Applicants also note that the claim 1 (from which claims 2, 3, 20, 47, 48, 50, 51, 53, 54, 56, and 57 depend) has been amended to no longer recite the term "coding region" (claims 4-7 do not recite "coding region") Accordingly, for at least this additional reason, claims 1-3, 20, 47, 48, 50, 51, 53, 54, 56, and 57 cannot be interpreted as encompassing the ribozymes of Breaker. In this regard, Applicants note that none of the ribozymes described in Breaker include sequence the expression of which is regulated by the ribozyme nor do the ribozymes or aptamers of Breaker regulate expression of any sequence. Thus, for at least these reasons, Breaker fails to

disclose every feature of claims 1-3, 20, 47, 48, 50, 51, 53, 54, 56, and 57. Accordingly, for at least these reasons, Breaker fails to anticipate claims 1-3, 20, 47, 48, 50, 51, 53, 54, 56, and 57.

Applicants also note that claims 1-3, 20, 47, 48, 50, 51, 53, 54, 56, and 57 require that the riboswitch regulate expression of the sequence operably linked to the riboswitch. Thus, claims 1-3, 20, 47, 48, 50, 51, 53, 54, 56, and 57 require a construct that is capable of expression of a sequence operably linked to the riboswitch. The ribozyme of Breaker does not include any sequence that is or can be expressed. Although the ribozyme of Breaker can cleave an RNA strand that forms part of the ribozyme, no part of the ribozyme structure of Breaker is expressed or can be expressed. Thus, for at least these additional reasons, Breaker fails to disclose every feature of the claimed constructs and riboswitches.

Although the Office Action mailed July 10, 2007 states that Breaker "teaches gene expression constructs" (page 8), the ribozyme constructs of Breaker do not regulate gene expression. Clarification is requested. To the extent that the rejection may be based on the speculation in Breaker about possible control of protein expression by RNA molecular switches, Breaker does not disclose or describe any present or operable allosteric ribozyme or "RNA molecular switch" that could control expression of a protein. In fact, the paragraph in which Breaker makes this speculation (first full paragraph on page 38) clearly indicates that the allosteric ribozymes needed and genetic control by such allosteric ribozymes did not presently exist. Further, Breaker makes it clear that obtaining such constructs and achieving such use would require additional work ("this application poses many challenges to ribozyme engineers"). Because Breaker fails to disclose ribozyme constructs that did or could control expression of any sequence, and because Breaker clearly indicates that such use lay in the future and would pose challenges, Breaker clearly fails to disclose this aspect of the claimed constructs. Accordingly, Breaker fails to disclose every feature of claims 1-3, 20, 47, 48, 50, 51, 53, 54, 56, and 57 and thus fails to anticipate claims 1-3, 20, 47, 48, 50, 51, 53, 54, 56, and 57.

With regard to claims 4-7, the claimed riboswitch is a non-natural derivative of a naturally-occurring riboswitch. The ribozyme of Breaker includes an aptamer that is not derived from a naturally-occurring riboswitch. Further, the ribozyme portion of the Breaker ribozyme is

not derived from a riboswitch, whether naturally-occurring or not. Rather, Breaker puts together an artificially created aptamer and a derivative of a ribozyme. Neither of these components is derived from a riboswitch. Thus, for at least these reasons, Breaker fails to disclose a riboswitch as claimed in claims 4-7.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A deposit order account charge made electronically in the amount of $1029.00, representing $555.00 for the fee for a small entity under 37 C.F.R. § 1.17(a)(3), $110.00 for the fee for a small entity under 37 C.F.R. § 1.16(h), and $364.00 for the fee for a small entity under 37 C.F.R. § 1.16(i), and a Request for Extension of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-4667.

Respectfully submitted,

ARNALL GOLDEN GREGORY LLP

/Robert A. Hodges/
Robert A. Hodges
Registration No. 41,074

ARNALL GOLDEN GREGORY LLP
Customer Number 53449
(404) 873-8500
(404) 873-8501 (fax)